

AMENDMENTS TO THE CLAIMS

Claims 1-3, 10-13, 19, 20, 34-36, 40-46, 48-55, 108, 109, 113-116, 118-120 and 122-126 are pending. Claim 5 is cancelled herein without prejudice or disclaimer. Please amend claims 1, 12, 13 and 19 as indicated below. This listing of claims replaces all prior versions, and listings of claims, in the application.

LISTING OF CLAIMS:

1. (Currently amended) An isolated, substantially purified single-chain polypeptide, comprising consisting of a protease domain of a type-II membrane-type serine protease (MTSP) or a catalytically active fragment thereof as a single chain, wherein wherein: ~~the MTSP protease domain or catalytically active fragment thereof is the only portion of the single chain polypeptide from the MTSP, and~~ _____
the MTSP protease domain or catalytically active fragment thereof has serine protease activity as a single chain.

2. (Previously presented) The substantially purified polypeptide of claim 1, wherein the MTSP is not expressed on endothelial cells.

3. (Original) The substantially purified polypeptide of claim 1, wherein the MTSP is not expressed on normal endothelial cells *in vivo*.

4. - 9. (Cancelled).

10. (Withdrawn) The substantially purified polypeptide of claim 1, wherein the MTSP portion has an N-terminus that comprises IVNG, ILGG, VGLL or ILGG.

11. (Previously Presented) The substantially purified polypeptide of claim 1, wherein the MTSP is selected from among MTSP1, MTSP3, MTSP4 and MTSP6.

12. (Withdrawn) The substantially purified polypeptide of claim 1, wherein the MTSP protease domain consists of has a sequence of amino acid residues set forth as selected from among amino acids 615-855 of SEQ ID No. 2, as amino acid residues 205-437 of SEQ ID NO. 4, as the amino acid residues in set forth as SEQ ID No. 6 or as amino acids 217-443 in SEQ ID No. 12.

13. (Withdrawn) The substantially purified polypeptide of claim 1 that has at least about 95% sequence identity with a protease domain consisting of a whose sequence of amino acid residues is set forth as selected from among amino acid residues acids 615-855 of SEQ ID No. 2, as amino acid residues 205-437 of SEQ ID NO. 4, as the amino acid residues in acids set forth as SEQ ID No. 6, or as and amino acid residues acids 217-443 in SEQ ID No. 12.

Claims 14 - 18 (Cancelled).

19. (Currently amended) The polypeptide of claim 1, wherein a free Cys in the protease domain is replaced with another amino acid, ~~whereby~~ wherein the resulting polypeptide ~~exhibits proteolytic~~ retains serine protease activity.

20. (Previously presented) The polypeptide of claim 1, wherein a free Cys in the protease domain is replaced with a serine.

Claims 21- 33 (Cancelled).

34. (Withdrawn) The polypeptide of claim 1, wherein the MTSP is selected from among corin, MTSP1, enteropeptidase, human airway trypsin-like protease (HAT), TMPRSS2, and TMPRSS4.

35. (Previously presented) A conjugate, comprising:

- a) a polypeptide of claim 1, and
- b) a targeting agent linked to the protein directly or via a linker, wherein the conjugate has serine protease activity.

36. (Original) The conjugate of claim 35, wherein the targeting agent permits

- i) affinity isolation or purification of the conjugate;
- ii) attachment of the conjugate to a surface;
- iii) detection of the conjugate; or
- iv) targeted delivery to a selected tissue or cell.

Claims 37 – 39 (Cancelled)

40. (Previously presented) A solid support comprising two or more polypeptides of claim 1 linked thereto either directly or via a linker.

41. (Previously presented) The support of claim 40, wherein the polypeptides comprise an array.

42. (Previously presented) The support of claim 41, wherein the array comprises polypeptides having different MTSP protease domains.

43. (Withdrawn) A method for identifying candidate anti-tumor compounds that inhibit the protease activity of an MTSP, comprising:

contacting a polypeptide of claim 1 with a substrate proteolytically cleaved by the MTSP, and, either simultaneously, before or after, adding a test compound or plurality thereof; measuring the amount of substrate cleaved in the presence of the test compound; and selecting compounds that change the amount cleaved compared to a control, whereby compounds that modulate the activity of the MTSP are identified.

44. (Withdrawn) The method of claim 43, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

45. (Withdrawn) The method of claim 43, wherein a plurality of the test compounds are screened simultaneously.

46. (Withdrawn) The method of claim 43, wherein the change in the amount cleaved is assessed by comparing the amount cleaved in the presence of the test compound with the amount in the absence of the test compound.

47. (Cancelled)

48. (Withdrawn) The method of claim 43, wherein a plurality of the polypeptides are linked to a solid support, either directly or via a linker.

49. (Withdrawn) The method of claim 43, wherein the polypeptides comprise an array.

50. (Withdrawn) The method of claim 43, wherein the polypeptides comprise a plurality of different MTSP proteases.

51. (Withdrawn) A method of identifying a compound that specifically binds to a single chain protease domain of an MTSP, comprising:

contacting a polypeptide of claim 1 with a test compound or plurality thereof under conditions conducive to binding thereof; and

identifying compounds that specifically bind to the MTSP single chain protease domain or compounds that inhibit binding of a compound known to bind to the MTSP single chain protease domain, wherein the known compound is contacted with the polypeptide before, simultaneously with or after the test compound.

52. (Withdrawn) The method of claims 51, wherein the polypeptide is linked either directly or indirectly via a linker to a solid support.

53. (Withdrawn) The method of claim 51, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

54. (Withdrawn) The method of claim 51, wherein a plurality of the test substances are screened for simultaneously.

55. (Withdrawn) The method of claim 52, wherein a plurality of the polypeptides are linked to a solid support.

56. -107. (Cancelled).

108. (Previously presented) A conjugate, comprising:

a) an MTSP3 or an MTSP4 or the MTSP6 of claim 12; and

b) a targeting agent linked to the protein directly or via a linker.

109. (Previously presented) The conjugate of claim 108, wherein the targeting agent permits

- i) affinity isolation or purification of the conjugate;
- ii) attachment of the conjugate to a surface;
- iii) detection of the conjugate; or
- iv) targeted delivery to a selected tissue or cell.

Claims 110 – 112 (Cancelled).

113. (Previously presented) A solid support comprising two or more polypeptides of claim 12 linked thereto either directly or via a linker

114. (Previously presented) The support of claim 113, wherein the polypeptides comprise an array.

115. (Withdrawn) A method for identifying compounds that modulate the protease activity of an MTSP of claim 1, comprising:

contacting the MTSP of claim 1 with a substrate proteolytically cleaved by the MTSP, and, either simultaneously, before or after, adding a test compound or plurality thereof; measuring the amount of substrate cleaved in the presence of the test compound; and selecting compounds that change the amount cleaved compared to a control, whereby compounds that modulate the activity of the MTSP are identified.

116. (Withdrawn) The method of claim 115, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

117. (Cancelled).

118. (Withdrawn) The method of claim 115, wherein the change in the amount cleaved is assessed by comparing the amount cleaved in the presence of the test compound with the amount in the absence of the test compound.

119. (Withdrawn) The method of claim 115, wherein a plurality of the test substances are screened for simultaneously.

120. (Withdrawn) The method of claim 119, wherein a plurality of the polypeptides are linked to a solid support.

121. (Cancelled).

122. (Withdrawn) A method of identifying a compound that specifically binds to an MTSP protease domain, comprising:

contacting an MTSP protease domain of claim 12 with a test compound or plurality thereof under conditions conducive to binding thereof; and

identifying compounds that specifically bind to the MTSP.

123. (Withdrawn) The method of claim 122, wherein the polypeptide is linked either directly or indirectly via a linker to a solid support.

124. (Withdrawn) The method of claim 122, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

125. (Withdrawn) The method of claim 122, wherein a plurality of the test substances are screened for simultaneously.

126. (Withdrawn) The method of claim 125, wherein a plurality of the polypeptides are linked to a solid support.

127. – 137. (Cancelled).